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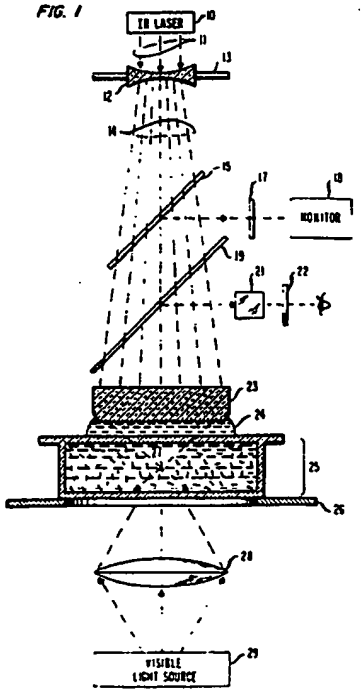
(54) Non-destructive optical trap for biological particles and method of doing same.

(57) Biological particles are successfully trapped in a single-beam gradient force trap using an infrared laser. The high numerical aperture lens objective in the trap is also used for simultaneous viewing.

Several modes of trapping operation are presented.

FIG. 1



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energy in the trap by the confined particle may lead to particle annihilation or a significant loss of particle motility. Also, as the wavelength of the light beam is varied to avoid the aforementioned problem, the intensity of the optical trap may be sufficiently decreased so as to be rendered ineffective for the particles of interest. While the wavelength selected may be sufficient for effective operation of the optical trap, it may be at a wavelength which is absorbed by the medium surrounding the particles and, therefore, which leads to heat generation within the cell. Clearly, many factors must be considered when selecting the operation wavelength for the optical trap.

In the prior optical trap experiments reported in the literature, particle sensitivity has not been an issue. This is generally attributed to the fact that dielectric particles have homogeneous compositions and uniformly regular shapes so that it is straightforward to observe the effect of the trap on one particle or portion of a particle and accurately predict the effect on other particles or on other portions of the same dielectric particle. for biological particles, sensitivity of the particles is extremely important. Biological particles have heterogeneous compositions and irregular shapes. Hence, the effect of the trap on one part of a biological particle is in no way determinative of the effect in another portion of the same particle.

FIG. 1 shows a cross-sectional schematic diagram of apparatus for creating a single-beam gradient force optical trap in accordance with the principles of this invention. IR laser 10 is a standard laser emitting a coherent light beam substantially in the infrared range of wavelengths, for example, 0.8 μm to 1.8 μm.

Light beam 11 from IR laser 10 impinges upon a combination of optics elements for focusing the light beam with a sufficient degree of convergence to form a single-beam gradient force optical trap for confining biological particles at a desired position. The combination of optics elements includes an adjustably mounted diverging lens 12 and a high convergence lens 23.

Lens 12 is adjustable in any of three dimensions (x, y, z) by manipulating adjustable mount 13. It is important that lens 12 expand the spot size of light beam 11 to cover a substantial area on the surface of lens 23. As shown in FIG. 1, diverging light beam 14 impinges on a large portion of the facing surface of lens 23 so that relatively high intensity of beam 14 fills the aperture of lens 23. In order to create the forces required for operation of the single-beam gradient force optical trap, it is desirable that lens 23 be capable of focusing to a spot size less than λ approaching $\lambda/2$. In an example from experimental practice, lens 23 is a strong or high convergence water immersion microscope objective lens having a numerical aperture of approximately 1.25 (measured in water). wherein the numerical aperture is defined as the refractive index for the medium multiplied by the sine of the half angle covered by the converging light beam. Element 24 depicts the liquid (water or oil) in which lens 23 is immersed for improved optical coupling into cell 25.

The optical trap is shown within cell 25 with particle 27 in the trap. Particle 27 is suspended in a liquid medium such as water, for example, which is enclosed by cell 25. Cell 25 is a transparent enclosure for enclosing the suspended biological particles or a transparent slide from which particle containing droplets can be hung. In one example, cell 25 has dimensions of 1 cm. x 3 cm. x 100 μm.

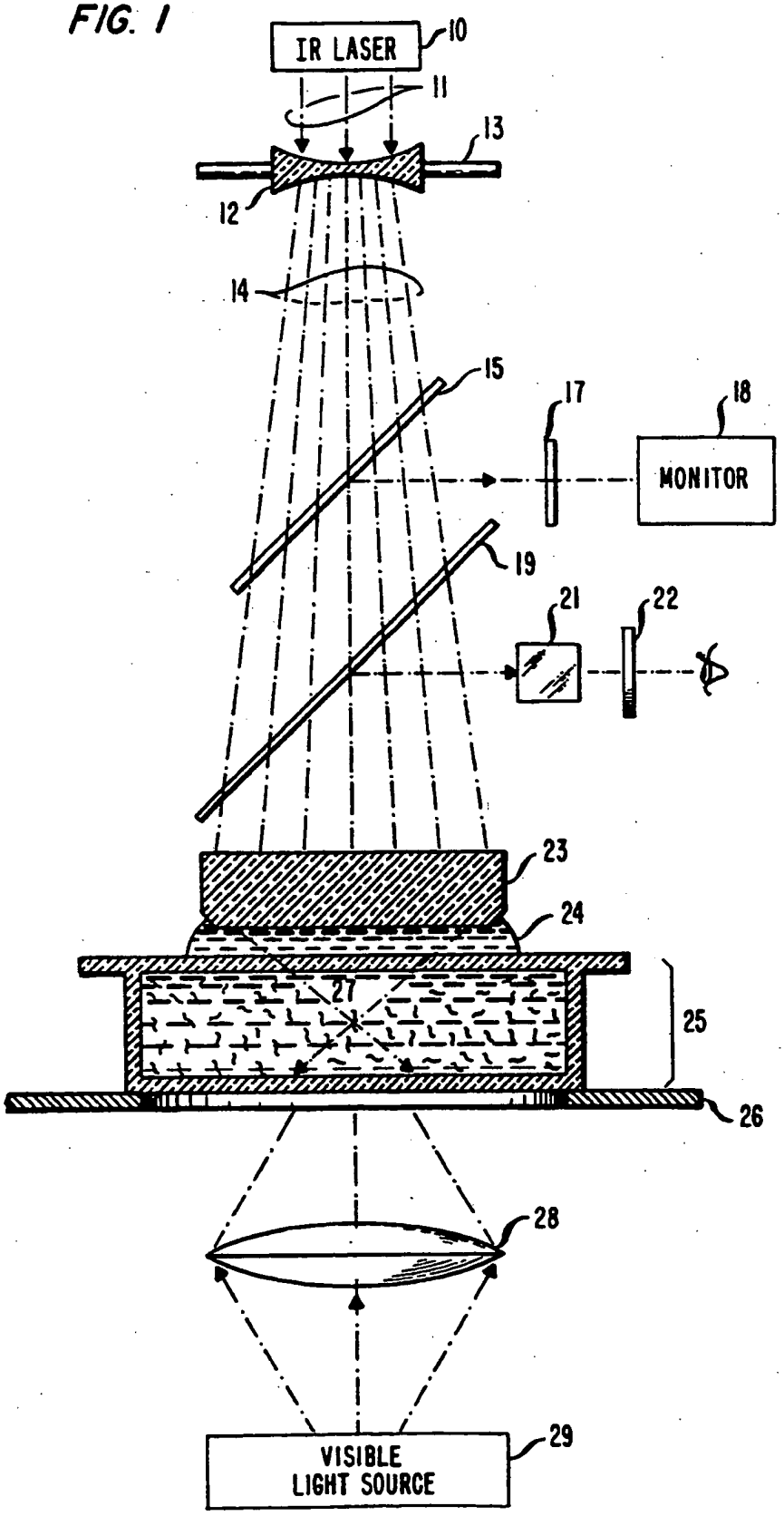
The position of cell 25 is adjustable in three dimensions (x, y, z) by the use of adjustable mount 26. In practice, mount 26 is useful in locating and manipulating the biological particles.

Viewing of biological particles in the trap is accomplished directly or through the use of a monitor. While other types of viewing such as viewing directly in cell 25 are possible, it is an added feature of the present invention the viewing is accomplished through the same lens objective which simultaneously creates the optical trap.

Illumination for viewing is provided by visible light source 29 and is projected through converging lens 28 onto the particles in the field of view. High resolution viewing occurs with the aid of lens 23 through which the visible light passes toward either the eyepiece or the monitor 18. For direct viewing, visible light shown as a dashed line is reflected from beam splitter 19 to microscope eyepiece 21. Infrared blocking filter 22 is placed in front of eyepiece 21 to isolate the viewing optics (viewer's eye) from back reflections from cell 25. For monitoring, the visible light passes through beam splitter 19 and is reflected from beam splitter 15 toward infrared blocking filter 17 and finally monitor 18. Infrared blocking filter 17 isolates the monitor from back reflections from cell 25.

In FIG. 2, the apparatus shown in FIG. 1 is augmented by a second infrared laser source and optics to create a second single-beam gradient force optical trap in cell 25. Infrared laser source 30 generates light beam 31 impinging on adjustably mounted diverging lens 32. Lens 32 causes beam 31 to emerge in a diverging pattern as light beam 34. Adjustment of lens 32 is accomplished in three dimensions (x, y, z) via adjustable mount 33. Light beam 34 is reflected by mirror 35 which coincidently permits transmission of light beam 14. This would occur by judiciously choosing different wavelengths of operation for the separate laser sources. On the other hand, element 35 can be realized as a beam splitter which would reflect

FIG. 1


IR LASER
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MONITOR
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23
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VISIBLE
LIGHT SOURCE
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FIG. 3

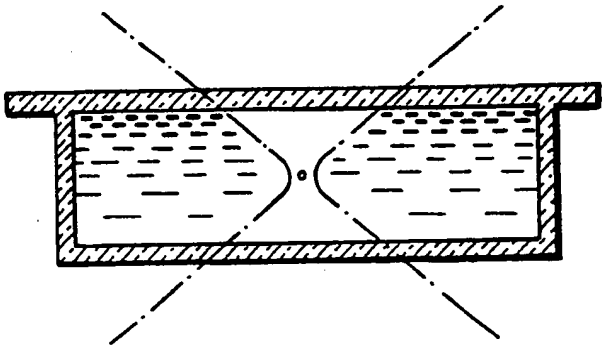

FIG. 4

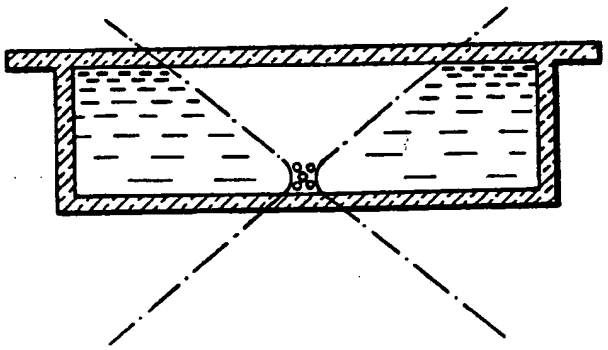

FIG. 5